

Amendments to the Specification:

Please replace the paragraph beginning at page 1, line 26 with the following:

A successful determination of the concentration of an analyte requires proper thermal and optical contact between an optical probe and the surface of the tissue. Example of such devices are described U. S. Patent No. 6,241,663; U. S. Patent No. 6,353,226; U. S. Patent No. 6,526,298; U. S. Patent No. 6,615,061; U. S. Patent No. 6,662,030; U. S. Patent No. 6,662,031; WO 99/59464; WO 2002/060320A1; ~~WO 2002/82989A1~~ WO 2002/082989A1; U.S. Serial Nos. 09/419,461, filed October 15, 1999, and 09/834,440, filed April 13, 2001; and Khalil, et al., "Temperature modulation of the visible and near infrared absorption and scattering coefficients of intact human skin", *J. Biomedical Optics*, 8(2), 191-205 (April 2003); Yeh, et al., "Near-infrared thermo-optical response of the localized reflectance of intact diabetic and non-diabetic human skin", *J. Biomedical Optics*, 8(3), 534-544 (July 2003); and Yeh, et al., "Monitoring Blood Glucose Changes in Cutaneous Tissue by Temperature-modulated Localized Reflectance Measurements", *Clinical Chemistry* 49:6 924-934 (2003).

Please replace the paragraph beginning at page 7, line 16 with the following:

As used herein, the term "trend" means the general direction of the magnitude of the signal as a function of time; if the signal increases, the trend is upward; if the signal decreases the trend is downward. The term "probe" means an element that comprises at least one sensor for detecting and preferably measuring optical signals. The probe contacts the tissue during a measurement. In a preferred embodiment, the probe comprises a combined optical/thermal head in the form of an aluminum temperature-controlled

disc having a fiber-optic bundle at the center of the disc. The term "sensor" means a device that detects a signal. The term "artifact" refers to a feature in the data that can result in an erroneous calculation of the concentration of the analyte. The artifact distorts the actual trend of the intensity of the radiation emitted over a period of time. The expression "motion artifact" refers to an artifact occurring within a brief period of time resulting from accidental movement of the optical probe or the tissue. A motion artifact typically causes a large perturbation in the optical data. The expression "intact human tissue" means a non-excised portion of tissue that is a part of an organ of a living patient. The expression "true data" means data that excludes motion artifacts. True data represents the actual signal that should be measured from intact human tissue. The expression "brief period of time" means the period of time required for making a measurement, which typically ranges up to three minutes. ~~The expressions "determine the concentration of an analyte", "determination of the concentration of an analyte", "determining the concentration of an analyte", and the like, include not only the determination of the concentration of a substance in a tissue, but also the determination of values of various physiological parameters, including, but not limited to, value of hematocrit, level of blood pressure.~~

Please replace the paragraph beginning at page 11, line 17 with the following:

The algorithm incorporates a time scale via a set of equations that process optical data from the apparatus. The equations, which are described below, are used to calculate a novel moving average value, $A(i)$, for test data from each individual channel of the apparatus. The data in a given time scale consists of the current data point (for which the value of $A(i)$ is being calculated) plus a fixed quantity of previously collected data points (N) selected for the calculations. For example, the algorithm can be applied over a time scale of 60 seconds

to data that are recorded every 5 seconds; hence, $N = 60/5 = 12$ data points. By selecting N in this manner, the values of $A(i)$ will closely follow the values of a series of data points recorded during a normal thermal/optical interaction between the tissue and the probe. Only when an artifact occurs will the value(s) of $A(i)$ begin to differ significantly from the values of the series of data points. FIG. 4 shows the indication of an artifact. An artifact is deemed detected when the absolute difference between the value of a data point and the corresponding value of $A(i)$ exceeds a threshold value (D_c), which is specified by the operator. The operator selects an appropriate threshold value for each channel, such that all significant artifacts are detected, while other minor fluctuations (resulting from vasodilatation, random noise, etc.) are excluded. Optimum selection of the appropriate threshold value can be determined by performing comprehensive calibration experimentation with the probe on a population of patients. The number of patients (e.g., 20 patients) should be selected to produce a good statistical sample within the population in terms of the observed range of vasodilation, random noise, etc. Such a number preferably ranges from about 20 to about 100, based on experience with populations of patients that show statistically significant results. Furthermore, the number of measurement per patient (e.g., 10 to 100) should be chosen to produce a good statistical sample of the observed test-to-test variation of vasodilation, random noise, etc. Such a number preferably ranges from about 10 to about 100, based on ~~based on~~ experience with populations of patients that show statistically significant results.

Please replace the paragraph beginning at page 15, line 30 with the following:

The method of this invention can be used with apparatus described previously to detect artifacts in recorded optical data to immediately alert the user that ~~user that~~ a measurement may be

erroneous and that a repeat measurement is necessary. On-board software can be used to apply the method of this invention to each individual channel of data and to display the results in real-time on a computer screen display. This method of detection of artifacts is extremely useful for those instances in which the probe is accidentally moved during collection of data, the probe is improperly applied to the surface of the tissue, or any interfering substances come between the probe and the surface of the tissue. Interfering substances include, but are not limited to, body hair, moles, tattoos, scars, dirt, or any other materials that obstruct the light returning from the surface of the tissue and cause rapid perturbations in the recorded data.